

CLAIMS

1. An isolated polynucleotide encoding a protein, which modulates corticotropin releasing hormone (CRH) signaling said protein having an amino acid sequence selected from the group consisting of SEQ ID NO:46 and SEQ ID NO:48.
5
2. An isolated polynucleotide according to claim 1 wherein said polynucleotide is mRNA, DNA or cDNA.
10
3. An isolated polynucleotide encoding a protein, which modulates corticotropin releasing hormone (CRH) signaling said polynucleotide comprising a nucleic acid sequence selected from the group consisting of SEQ ID NO:45, SEQ ID NO:47 and SEQ ID NO:49.
15
4. An isolated polynucleotide encoding a protein, which modulates corticotropin releasing hormone (CRH) signaling said polynucleotide consisting of a nucleic acid sequence selected from the group consisting of SEQ ID NO:45, SEQ ID NO:47 and SEQ ID NO:49.
20
5. An isolated polypeptide encoding a protein, which modulates corticotropin releasing hormone (CRH) signaling said protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:46 and SEQ ID NO:48.
25
6. A vector comprising an isolated polynucleotide according to any one of claims 1 to 4.
7. A vector according to claim 6 wherein the polynucleotide is operably linked to an expression control sequence.
30

8. A host cell capable of expressing a protein, which modulates corticotropin releasing hormone (CRH) signaling, said protein having an amino acid sequence selected from the group consisting of SEQ ID NO:46 and SEQ ID NO:48.
- 5
9. A host cell according to claim 8 transfected with a vector comprising a regulatory sequence.
10. A host cell according to claim 8 transfected with a vector according to claims 6 or 7.
- 10
11. A method for identifying a compound capable to alter the CRH signalling response in a cell, said method comprising;
- 15
- a) contacting said cell with CRH in the presence and absence of said compound;
- b) determine the amount of at least one protein that modulates corticotropin releasing hormone (CRH) signaling in said cell; and
- c) compare the amount of said protein in the presence and absence of said compound;
- whereby the protein that modulates corticotropin releasing hormone (CRH) signaling is being selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.
- 20
- 25
12. A method according to claim 11 wherein the cell is a eukaryotic cell such as the murine pituitary corticotroph-derived adenoma cell line AtT-20.
- 30
13. A method according to claims 11 or 12 wherein the amount of protein that modulates CRH signaling is being determined using an antibody which binds to a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ

ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

5

14. A method according to claims 11 or 12 wherein the amount of protein that modulates CRH signaling is being determined by assessing the level of gene transcription of a gene encoding an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

10

15

15. A method according to claim 14 wherein the level of gene transcription is being assessed using a probe which binds to a polynucleotide encoding an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

20

25

16. A method according to claims 14 or 15 wherein the level of gene expression is analysed using microarray technology.

17. A method according to claim 16 wherein the level of gene expression is assessed using an array of oligonucleotide probes that bind to the polynucleotides encoding the group of polypeptides having the amino acid sequences SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

30

35

NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

18. A method for identifying a compound capable to alter the CRH signalling response in a cell, said method comprising;
- 5 a) contacting said cell in the presence and absence of a test compound; and
- b) determine the expression levels of the genes encoding the polypeptides with the amino acid sequences SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.
- 10
19. A method according to claim 18 wherein the expression levels of the genes are determined using an array of oligonucleotide probes that bind to the polynucleotides having the nucleic acid sequences SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31, SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:47 and SEQ ID NO:49.
- 15
20. A method for identifying a compound capable to alter the CRH signalling response activity in a cell, said method comprising;
- 25 a) contacting a cell which expresses at least one protein comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48, with said test compound; and
- 30

b) compare the CRH response activity of said cell in the presence and absence of said compound.

21. A method according to claim 20 wherein the cell expresses the group of proteins having the amino acid sequences SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.
22. A method according to claim 21, wherein the CRH response activity is being assessed as changes in transcription at the gene level.
23. A method according to claims 21 or 22, wherein the CRH response activity is being assessed using microarray technology.
24. A method according to any one of claims 20 to 23 wherein the cell is host cell capable to express at least one protein having an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.
25. A method according to claim 24 wherein the host cell is transfected with at least one vector comprising a regulatory sequence.
26. A method according to claim 24 wherein the host cell is transfected with at least one vector comprising a polynucleotide sequence encoding an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID

NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

5 27. A method of diagnosing CRH induced depression in an individual said method comprising;

 a) obtaining a biological sample of said individual; and

 b) determine the amount of at least one protein that modulates corticotropin releasing hormone (CRH) signaling in said biological sample;

10 whereby the protein that modulates corticotropin releasing hormone (CRH) signaling is being selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

20 28. A method according to claim 27 wherein the biological sample is a bodily fluid or tissue sample

25 29. A method according to claims 27 or 28 wherein wherein the amount of protein that modulates CRH signaling is being determined using an antibody which binds to a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

30 30. A method according to claims 27 or 28 wherein the amount of protein that modulates CRH signaling is being determined by assessing the level of gene transcription of a gene encoding an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID

5 NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

10 31. A method according to claim 30 wherein the level of gene transcription is being assessed using a probe which binds to a polynucleotide encoding an amino acid sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

15

32. A method according to claims 30 or 31 wherein the level of gene transcription is analysed using microarray technology.

20 33. A method according to claim 32 wherein the level of gene transcription is analysed using an array of oligonucleotide probes that bind to the polynucleotides encoding the group of polypeptides having the amino acid sequences SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:14, SEQ ID NO:16, SEQ ID NO:18, SEQ ID NO:20, SEQ ID NO:22, SEQ ID NO:24, SEQ ID NO:26, SEQ ID NO:28, SEQ ID NO:30, SEQ ID NO:32, SEQ ID NO:34, SEQ ID NO:36, SEQ ID NO:38, SEQ ID NO:40, SEQ ID NO:42, SEQ ID NO:44, SEQ ID NO:46 and SEQ ID NO:48.

25

30 34. A method according to claim 32 wherein the level of gene transcription is analysed using an array of oligonucleotide probes that bind to that bind to the polynucleotides having the nucleic acid sequences SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:17, SEQ ID NO:19, SEQ ID NO:21, SEQ ID NO:23, SEQ ID NO:25, SEQ ID NO:27, SEQ ID NO:29, SEQ ID NO:31,

SEQ ID NO:33, SEQ ID NO:35, SEQ ID NO:37, SEQ ID NO:39, SEQ ID NO:41, SEQ ID NO:43, SEQ ID NO:45, SEQ ID NO:47 and SEQ ID NO:49.